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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,691	04/14/2004	Steven J. Soldin	31603-2053	5360

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TORYS LLP
79 WELLINGTON ST. WEST
SUITE 3000
TORONTO, ON M5K 1N2
CANADA

EXAMINER	
WALLENHORST, MAUREEN	
ART UNIT	**PAPER NUMBER**
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,691	SOLDIN, STEVEN J.	
	Examiner	Art Unit	
	Maureen M. Wallenhorst	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☒ Claim(s) *1-33* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

2. The abstract of the disclosure is objected to because of the inclusion of legal phraseology such as "comprise" and "comprising". Correction is required. See MPEP § 608.01(b).

3. Claims 1-33 are objected to because of the following informalities: In claims 1, 27, 28, 30 and 32, the full meaning for the abbreviation "DHEAs" should be recited, i.e. -- dehydroepiandrosterone sulphate (DHEAs)--. Appropriate correction is required.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-7, 9, 12-16, 18, 21, 25-29 and 32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Draisci et al (article from Journal of Chromatography A).

Draisci et al teach of a method for the quantitation of the steroid hormones 17-beta-19-nortestosterone, 17-beta-testosterone and progesterone in a blood serum/plasma or urine sample by the use of liquid chromatography-tandem mass spectrometry. In the method, a 2 mL sample of blood serum/plasma or urine (i.e. at least about 700 microliters, as recited in instant claim 9) is obtained that contains the hormones 17-beta-19-nortestosterone, 17-beta-testosterone and

progesterone, the sample is deproteinated and purified by solid phase extraction using a C-18 cartridge, eluted with methanol, and injected into a LC-MS-MS system. An injection valve equipped with a 5 microliter internal loop is used for injection of the sample into the LC-MS-MS system. The steroid hormones are separated from the sample by the liquid chromatography step, and analyzed using the mass spectrometer. Since the sample analyzed using the method taught by Draisci et al contains testosterone in addition to other steroids, it meets the limitation in the instant independent claims concerning analyzing a multitude of steroid hormones, wherein at least one of the multitude of steroid hormones comprises testosterone. The mass spectral analysis is performed on a mass spectrometer operating in the positive ion mode that is equipped with an atmospheric pressure chemical ionization (APCI) source. Draisci et al teach that the combination of liquid chromatography with tandem MS-MS offers a rapid, simplified and sensitive method for analyzing a multitude of steroid hormones in a blood serum/plasma or urine sample that involves simple extraction procedures and removes the need for derivatization reactions. See pages 511-513 in Draisci et al.

6. Claims 1-5, 9, 12-16, 18, 21, 25-29 and 32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Tiller et al (article from the Journal of Chromatography A).

Tiller et al teach of a method for the quantitation of steroids in a human plasma sample using liquid chromatography-tandem mass spectrometry. The method comprises the steps of obtaining a 1 mL aliquot of human plasma sample (i.e. at least about 700 microliters, as recited in instant claim 9), containing the hormones testosterone and hydrocortisone. The sample is deproteinated by solid phase extraction on a C-8 extraction column. The eluate is evaporated to dryness, spiked with internal standards for testosterone and hydrocortisone, reconstituted with

mobile phase and injected onto a C-18 column of a liquid chromatograph in order to separate the steroid hormones from the sample. The sample is then injected into a tandem mass spectrometer for analysis of the steroids. The MS-MS system operates using an atmospheric pressure chemical ionization (APCI) probe in the positive ion selection mode. Full scan MS-MS data are obtained for testosterone, hydrocortisone and their labeled internal standards. Since the sample analyzed using the method taught by Tiller et al contains testosterone in addition to other steroids, it meets the limitation in the instant independent claims concerning analyzing a multitude of steroid hormones, wherein at least one of the multitude of steroid hormones comprises testosterone. See pages 119-121 of Tiller et al.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Draisci et al or Tiller et al in view of Jonsson et al (article submitted in the IDS filed on November 30, 2006). For a teaching of Draisci et al and Tiller et al, see previous paragraphs in

this Office action. Draisci et al and Tiller et al fail to teach that the sample analyzed for steroid hormones can be a saliva sample, and fail to teach that the sample can be deproteinated and purified using acetonitrile.

Jonsson et al teach of a method and system for the determination of cortisol in saliva samples using liquid chromatography-electrospray tandem mass spectrometry. Saliva samples are spiked with a deuterium-labeled internal standard. Proteins are precipitated using acetonitrile, and then centrifuged. After centrifugation, the supernatant is applied to a C8 column. Mass spectrometry is performed on an API 3000 LC-MS-MS. See the abstract and experimental section on pages 64-65 of Jonsson et al.

Based upon the combination of either Draisci et al or Tiller et al with Jonsson et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to apply the liquid chromatography-tandem mass spectrometry method taught by either Draisci et al or Tiller et al to the analysis of steroid hormones in saliva samples since Jonsson et al teaches that steroid hormones such as cortisol can be detected in saliva samples using LC-MS-MS analysis, and the known technique of detecting steroid hormones in saliva samples was recognized as part of the ordinary capabilities of one skilled in the art. It also would have been obvious to one of ordinary skill in the art to deproteinate and purify the sample analyzed in the method taught by either Draisci et al or Tiller et al using acetonitrile followed by centrifugation since the simple substitution of one known method of deproteinization (i.e. combination with acetonitrile followed by centrifugation taught by Jonsson et al) for another known method (solid phase extraction taught by both Draisci et al and Tiller et al) would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

10. Claims 11 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Draisci et al or Tiller et al in view of Vogeser et al (article submitted in the IDS filed on November 30, 2006). For a teaching of Draisci et al and Tiller et al, see previous paragraphs in this Office action. Draisci et al and Tiller et al fail to teach that the sample can be deproteinated and purified using precipitation with an agent such as methanol, and fail to teach that the mass spectrometer uses multiple reaction monitoring.

Vogeser et al teach of a method and system for determining cortisol in serum samples. Serum samples are precipitated with a methanol/zinc sulfate solution containing deuterated cortisol as an internal standard. After vortexing, the samples are centrifuged and subject to HPLC chromatography on a C18 column. Figure 1 shows a column-switching scheme for an online extraction procedure. Electrospray atmospheric pressure ionization mass spectrometry in the positive mode is used. Multiple reaction monitoring is used. See the abstract and pages 944-945 of Vogeser et al.

Based upon the combination of either Draisci et al or Tiller et al with Vogeser et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to deproteinate and purify the sample analyzed in the method taught by either Draisci et al or Tiller et al using precipitation with an agent such as methanol since the simple substitution of one known method of deproteinization (i.e. precipitation with methanol taught by Vogeser et al) for another known method (solid phase extraction taught by both Draisci et al and Tiller et al) would have yielded predictable results to one of ordinary skill in the art at the time of the invention. It also would have been obvious to one of ordinary skill in the art to use multiple reaction monitoring in the mass spectral analysis taught by either Draisci et al or Tiller et al since the

known technique of multiple reaction monitoring in a mass spectrometer is recognized as part of the ordinary capabilities of one skilled in the art, as evidenced by the teaching of Vogeser et al.

11. Claims 17 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Draisci et al or Tiller et al in view of Alary (article submitted in the IDS filed on November 30, 2006). For a teaching of Draisci et al and Tiller et al, see previous paragraphs in this Office action. Draisci et al and Tiller et al fail to teach that the liquid chromatography-tandem mass spectrometer is equipped with an atmospheric pressure photoionization source.

Alary teaches that multiple steroid compounds in a sample can be advantageously analyzed using LC-MS/MS analysis equipped with an atmospheric pressure photoionization source. A multitude of steroid hormones including testosterone and ethynyl estradiol are analyzed on an API 3000 LC/MS/MS system having a photoionization source. Alary teaches that the photoionzation source produces enhanced and improved signals over those obtained using a conventional atmospheric pressure chemical ionization source (APCI). See the entire Alary article.

Based on the combination of either Draisci et al or Tiller et al with Alary, it would have been obvious to one of ordinary skill in the art to use an atmospheric pressure photoionization source in the mass spectrometer taught by either Draisci et al or Tiller et al in place of the atmospheric pressure chemical ionization source (APCI) since Alary teaches that a photoionization source in a mass spectrometer produces enhanced and improved results in a steroid hormone analysis as compared to a APCI source.

12. Claims 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Draisci et al or Tiller et al in view of Fredline et al (article submitted in the IDS filed on

November 30, 2006). For a teaching of Draisci et al and Tiller et al, see previous paragraphs in this Office action. Draisci et al and Tiller et al fail to teach of operating the mass spectrometer in the negative ion mode using selected ion monitoring.

Fredline et al teach of a method and system for the determination of aldosterone in samples of plasma or blood. Aliquots of 2 ml are extracted and deproteinated with dichloro-methane/diethyl ether, containing an internal standard. The sample is applied to a liquid chromatography system and analyzed using a tandem mass spectrometer in a selected reaction-monitoring mode. An atmospheric pressure chemical ionization interface is used in a negative ionization mode. See the abstract and pages 309-310 of Fredline et al.

Based upon the combination of either Draisci et al or Tiller et al with Fredline et al, it would have been obvious to one of ordinary skill in the art to operate the mass spectrometer taught by either Draisci et al or Tiller et al in the negative ion mode using selected ion monitoring since the known techniques of a negative ion mode and selected ion monitoring in a mass spectrometer is recognized as part of the ordinary capabilities of one skilled in the art, as evidenced by the teaching of Fredline et al.

13. Claims 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Draisci et al or Tiller et al. For a teaching of Draisci et al and Tiller et al, see previous paragraphs in this Office action.

Both Draisci et al and Tiller et al fail to teach of incorporating all of the needed/required reagents and instrumentation for analyzing steroid hormones in a biological sample into a kit form. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate all of the needed/required reagents and instrumentation required

for analyzing steroid hormones in accordance with the methods taught by either Draisci et al or Tiller et al in a kit form so as to make the methods more convenient and easy to perform by having all of the necessary components in one centralized location, thus facilitating the quick and efficient analysis of steroid hormones without having to take extra time to assemble the various reagents and instrumentation required.

14. Applicant's arguments with respect to claims 1-33 have been considered but are moot in view of the new ground(s) of rejection.

The previous objection to the abstract made in the last Office action mailed on May 1, 2007 has been maintained since Applicant's proposed amendments to the abstract in the "Remarks" section of the response received on October 1, 2007 have not been entered. In order for these amendments to be properly entered, the amended abstract should be placed in a separate section of the response with the heading "Amendment of the Abstract".

The previous rejections of the claims under 35 USC 112, second paragraph have been withdrawn in view of Applicant's amendments to the claims. The previous rejection of claims 32-33 under 35 USC 101 has also been withdrawn in view of the amendments made to these claims. All of the previous grounds of rejection of the claims under 35 USC 102 and 35 USC 103 using the references to Kissmeyer et al, Jonsson et al, Kao et al, Fredline et al, Leinonen et al and Vogeser et al have been withdrawn in view of the amendments made to the claims. Therefore, the Examiner will not respond to the arguments set forth by Applicant concerning these references. New grounds of rejection for the amended claims under 35 USC 102 and 35 USC 103 are made herein, as necessitated by Applicant's amendments to the claims.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Thursday from 6:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1797

mmw

November 27, 2007

Maureen M. Wallenhorst
MAUREEN M. WALLENHORST
PRIMARY EXAMINER
GROUP 1700